In re Application of: Jerachmiel Appelbaum
Serial No.: 10/550,681
Filed: September 26, 2005
Office Action Mailing Date: January 29, 2008

Examiner: Benjamin J. Packard
Group Art Unit: 4173
Attorney Docket: 30667

In the claims:

1. (Withdrawn) A composition for inhibiting the pathological activities of matrix metalloproteinases comprising an effective amount of NNN`N`-Tetrakis- (2-pyridyl-methyl)-ethylenediamine, (TPEN) and a pharmaceutically acceptable carrier.

2. (Withdrawn) A composition for inhibiting the pathological activities of matrix metalloproteinases as in claim 1, wherein the TPEN is in a concentration of 0.001-100 micromolar.

3. (Withdrawn) A composition for inhibiting the pathological activities of matrix metalloproteinases as in claim 1, where the active substance is a derivative, metal complexes and other forms of complexes of TPEN, including but not limited to ethylendiamine, diethylenetriamine, triethylenetetramine, triethylenediamine, tetraethylenep entamine, aminoethylethanol amine, aminoethylpiperazine, pentaethylenehexamine, triethylenetetramine-hydrochloride, tetraethylenepentamine-hydrochloride, pentaethylenehexamine-hydrochloride, tetraethylpentamine, captopril, penicilamine and transition metal binding peptides, wherein the composition is in concentration, but not limited to, of 000.1-100 micromolar.

4. (Withdrawn) A use of TPEN for the manufacture of a pharmaceutical composition for the treatment or prevention of pathological conditions influenced by the action of matrix metalloproteinases (MMPs).

5. (Withdrawn) The use, according to claim 3, wherein the disease influenced by the action of MMPs is atherosclerosis, corneal ulceration, emphysema,astma, osteoarthritis, chondrolitis and chondrosarcoma, osteoporosis, rheumatoid arthritis and other inflammatory disorders, autoimmune diseases, ulcerative colitis, primary malignancy, various types of carcinoma hodgkin's disease , various lymphomas and other hematological diseases, tumor invasion metastasis, angiogenesis and vasculogenesis, ischemia-reperfusion injury, stroke, acute MI,

coronary artery diseases and thrombolysis-associated hemorrhagic transformation, neurodegenerative diseases, Alzheimer's disease, Multiple Sclerosis, glaucoma, cataract and optic-nerve trama, brain-trauma, vascular thrombolysis and restenosis, aortic and blood vessels aneurism ,types of vasculitis as Kawasaki disease, ischemic heart and lung diseases, apoptosis, diabetes, digestive system disorders, organ rejection, infectious diseases, and mucosal pathogens such as N gonorrhoeae, P.gingivalis and other periodontal diseases, and sepsis,chronic wound and granulomas.

6. (Withdrawn) The use, according to claim 1, wherein the pharmaceutical composition is formulated for oral, parenteral or intradermal administration.

7. (Withdrawn) The use according to claim 1, wherein the pharmaceutical composition is formulated as a single pharmaceutical composition.

8. (Withdrawn) A composition for inhibiting the pathological activities of matrix metalloproteinases as in claim 1, wherein the TPEN is in the form of a metal complex formed with a metal.

9. (Withdrawn) A composition according to claim 8, wherein the metal is an inert metal.

10. (Withdrawn) A composition according to claim 8, wherein the metal complex is also for use in scavenging free radicals.

11. (Withdrawn) A use of TPEN as an anti-angiogenic agent in a pharmaceutical composition.

12. (Withdrawn) A use of TPEN as an anti-metastatic agent in a pharmaceutical composition.

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13. (Withdrawn) A use of TPEN as an anthrax-anti toxin.

14. (Withdrawn) A use of TPEN for inhibiting the spread of cancer in organs, cells, and tissue of the body.

15. (Withdrawn) A use of TPEN for the inhibition or prevention of ischemia and reperfusion injury in organs, cells, and tissues of the body where MMP activity plays a role.

16. (Withdrawn) A composition for inhibiting the pathological activities of matrix metalloproteinases comprising an effective amount of a highly specific metal chelator and a pharmaceutically acceptable carrier.

17. (Withdrawn) The composition, according to claim 16, wherein the metal chelator is a high affinity Zn^{2+} or Cu^{2+} polyamine chelating agent.

18. (Withdrawn) The composition, according to claim 17, wherein the polyamine chelating agent is selected from the group consisting of ethylendiamine, diethylenetriamine, triethylenetetramine, triethylenediamine, tetraethylenep entamine, aminoethylethanol amine, aminoethylpiperazine, pentaethylenehexamine, triethylenetetramine-hydrochloride, tetraethylenepentamine-hydrochloride, pentaethylenehexamine-hydrochloride, tetraethylpentamine, captopril, penicilamine and transition metal binding peptides.

19. (Canceled)

20. (Currently Amended) A method of treating a subject having a pathological condition influenced by the action of MMP, the method comprising administering to the subject an amount of TPEN or a TPEN derivative selected from the group consisting of ethylendiamine, diethylenetriamine, triethylenetetramine, triethylenediamine, tetraethylenepentamine, aminoethylethanol amine,

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aminoethylpiperazine, pentaethylenehexamine, triethylenetetramine-hydrochloride, tetraethylenepentamine-hydrochloride, pentaethylenehexamine-hydrochloride, tetraethylpentamine, captopril, penicilamine and transition metal binding peptides, ~~or any one of its derivatives~~ effective to treat or prevent the pathological condition, the pathological condition being selected from the group consisting of atherosclerosis, corneal ulceration, emphysema, asthma, osteoarthritis, chondrolitis and chondrosarcoma, osteoporosis, rheumatoid arthritis and other inflammatory disorders, autoimmune diseases, ulcerative colitis, primary malignancy, various types of carcinoma hodgkin's disease, various lymphomas and other hematological diseases, tumor invasion metastasis, angiogenesis and vasculogenesis, stroke, acute MI, coronary artery diseases and thrombolysis-associated hemorrhagic transformation, neurodegenerative diseases, Alzheimer's disease, Multiple Sclerosis, glaucoma, cataract and optic-nerve trauma, brain-trauma, vascular thrombolysis and restenosis, aortic and blood vessels aneurism, types of vasculitis as Kawasaki disease, ischemic heart and lung diseases, apoptosis, diabetes, digestive system disorders, organ rejection, infectious diseases, and mucosal pathogens such as N gonorrhoeae, P. gingivalis and other periodontal diseases, sepsis, chronic wound and granulomas.

21. (Canceled)

22. (Currently Amended) A method according to claim ~~21~~20, wherein the generation and/or action of MMP is induced and/or influenced by Nitros-Oxide (NO) and/or free radicals..

23. (Currently Amended) A method according to claim 20, being for ~~of~~ treating a subject having or suspected of having a pathological condition influenced by the action of Cyclooxiygenases, endonucleases, Metallopeptidases and 5-epoxygenase ~~comprising administering to the subject an amount of TPEN effective to inhibit the action of MMP~~.

24. (Currently Amended) A method according to claim ~~22~~23, wherein the cyclooxygenase is COX-1 or COX-2.

25. (Canceled)

26. (Withdrawn, Currently Amended) A method of treating a subject having or suspected of having a pathological condition influenced by the action of MMP, Cyclooxygenases, endonucleases, Metallopeptidases and 5-epoxygenase, the method comprising administering to the subject an amount of a complex formed between TPEN or a TPEN derivative - and a metal selected from the group consisting of selenium, gallium, molybdenum, manganese, iron, cobalt and ~~Germanium~~ germanium~~complex, or organic or inorganic Germanium alone~~, effective to inhibit the action of MMP.

27. (Withdrawn, Currently Amended) A method according to claim ~~25~~26, wherein the pathological condition influenced by the action of MMP is selected from the group of pathological conditions consisting of: atherosclerosis, corneal ulceration, emphysema, asthma, osteoarthritis, chondrolitis and chondrosarcoma, osteoporosis, rheumatoid arthritis and other inflammatory disorders, autoimmune diseases, ulcerative colitis, primary malignancy, various types of carcinoma hodgkin's disease-, various lymphomas and other hematological diseases, tumor invasion– metastasis, angiogenesis and vasculogenesis, ischemia-reperfusion injury, stroke, acute MI, coronary artery diseases and thrombolysis-associated hemorrhagic transformation, neurodegenerative diseases, Alzheimer's disease, Multiple Sclerosis, glaucoma, cataract and optic-nerve trauma, brain-trauma, vascular thrombolysis and restenosis, aortic and blood vessels aneurism-, types of vasculitis as Kawasaki disease, ischemic heart and lung diseases, apoptosis, diabetes, digestive system disorders, organ rejection, infectious diseases, and mucosal pathogens such as N gonorrhoeae, P. gingivalis and other periodontal diseases, ~~and~~ sepsis, chronic wound and granulomas.

28. (Withdrawn, Currently Amended) A method according to claim ~~25~~26, wherein ~~the Germanium is in complex with~~said TPEN derivative is a polyamine chelating agent selected from the group consisting of ethylendiamine, diethylenetriamine, triethylenetetramine, triethylenediamine, tetraethylenep~~e~~ntamine, aminoethylethanol amine, aminoethylpiperazine, pentaethylenehexamine, triethylenetetramine-hydrochloride, tetraethylenepentamine-hydrochloride, pentaethylenehexamine-hydrochloride, tetraethylpentamine, captopril, penicilamine and transition metal binding peptides.

29. (Withdrawn, Currently Amended) A method for inhibiting the lethal factor produced by toxigenic strains of anthrax bacteria, the method comprising exposing said lethal factor to an efficient amount of ~~a highly specific zinc chelator~~TPEN or a TPEN derivative selected from the group consisting of ethylendiamine, diethylenetriamine, triethylenetetramine, triethylenediamine, tetraethylenepentamine, aminoethylethanol amine, aminoethylpiperazine, pentaethylenehexamine, triethylenetetramine-hydrochloride, tetraethylenepentamine-hydrochloride, pentaethylenehexamine-hydrochloride, tetraethylpentamine, captopril, penicilamine and transition metal binding peptides.

30. (Withdrawn, Currently Amended) A method for inhibiting activities of fungi, bacteria, or plants that utilize zinc-dependent methionine synthetase (MetE), the method comprising delivering to an organism utilizing zinc-dependent methionine synthetase for metabolic activities an efficient amount of ~~a highly specific zinc chelator~~TPEN or a TPEN derivative selected from the group consisting of ethylendiamine, diethylenetriamine, triethylenetetramine, triethylenediamine, tetraethylenepentamine, aminoethylethanol amine, aminoethylpiperazine, pentaethylenehexamine, triethylenetetramine-hydrochloride, tetraethylenepentamine-hydrochloride, pentaethylenehexamine-hydrochloride, tetraethylpentamine, captopril, penicilamine and transition metal binding peptides.

31. (Withdrawn, Currently Amended) A method for inhibiting the activity of a zinc-dependent enzyme in- prokaryotic systems, the method comprising exposing a zinc-dependent enzyme to an efficient amount of ~~a highly specific zinc chelator~~TPEN or a TPEN derivative selected from the group consisting of ethylendiamine, diethylenetriamine, triethylenetetramine, triethylenediamine, tetraethylenepentamine, aminoethylethanol amine, aminoethylpiperazine, pentaethylenehexamine, triethylenetetramine-hydrochloride, tetraethylenepentamine-hydrochloride, pentaethylenehexamine-hydrochloride, tetraethylpentamine, captopril, penicilamine and transition metal binding peptides.

32. (Withdrawn, Currently Amended) A method ~~for inhibiting the activity of a zinc dependent enzymes~~according to claim 31, wherein – the zinc-dependent enzymes ~~are specifically~~is a- beta-lactamases.

33. (Canceled)